

REMARKS

Claims 28-39, 46 and 75 are in this application.

The Examiner states that claims 28-39, 46 and 75 are rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point and distinctly claim the subject matter which applicant regards as the invention. This is respectfully traversed.

According to the Examiner the claims are rendered vague and indefinite because they fail to recite a step for ingesting the colostrum and do not indicate when the fraction is ingested. The step of ingestion of the colostrum fraction is included in line 3 of claim 28. The fraction may be ingested anytime but logically it would be prior to when an improvement in physical work capacity is needed. It is administered over an "effective period" (see page 14, lines 18-21 and definition, page 14, lines 24- 27, see also page 17, lines 14-16).

The Examiner also indicates that it is unclear what kinds of subjects are intended by the claimed method. Claim 28 has been amended to define the subject as a human subject. Support for this amendment is found *inter alia* on page 4, lines 4-18.

Therefore, it is respectfully requested that this rejection be withdrawn.

The Examiner contends that claims 28-39, 46 and 75 are obvious in view of the following:

a) WO 97/16977;

- b) AU-A-63136/94;
- c) WO 97/43905;
- d) Clark et al.; and
- e) Ballard et al. (US 6,319,522).

All of these citations have been previously raised except for WO 97/43905 (Adler).

During the last interview and in the response to the Office Action of September 26, 2008, the relevancy of Clark *et al.* was discussed in detail and the Examiner at the time indicated that she would consider the argument that given the number of diseases and conditions that Clark *et al.* alleges to be treated and cured, one of skill in the art would not consider the reference to be believable. Applicants maintain that one of skill in the art would not find the reference to be credible and reliable given the large number of varied diseases and conditions that are supposedly treated or cured by ingestion of colostrum. As argued in the previous response the US Supreme Court in Daubert v. Merrell Dow, 509 US 579 (1993):

Faced with a proffer of expert scientific testimony under Rule 702, the trial judge, pursuant to Rule 104(a), must make a preliminary assessment of whether the testimony's underlying reasoning or methodology is scientifically valid and properly can be applied to the facts at issue. Many considerations will bear on the inquiry, including whether the theory or technique in question can be (and has been) tested, whether it has been subjected to peer review and publication, its known or potential error rate and the existence and maintenance of standards controlling its operation, and whether it has attracted widespread acceptance within a relevant scientific community. The inquiry is a flexible one, and its focus must be solely on principles and methodology, not on the conclusions that they generate. (Emphasis added)

Ordinarily, a key question to be answered in determining whether a theory or technique is scientific knowledge that will assist the trier of fact will be whether it can be (and has been) tested. "Scientific methodology today is based on generating hypotheses and testing them to see if they can be falsified; indeed, this methodology is what distinguishes science from other fields of human inquiry." Green, 645. See also C. Hempel, *Philosophy of Natural Science* 49 (1966) ("[T]he statements constituting a scientific explanation must be capable of empirical test"); K. Popper, *Conjectures and Refutations: The Growth of Scientific Knowledge* 37 (5th ed. [509 U.S. 579, 13] 1989) ("[T]he criterion of the scientific status of a theory is its falsifiability, or refutability, or testability").

The Examiner understands the invention to be as broad as administering colostrum prepared by ultrafiltration and spray drying and centrifugation and reconstitution. However, the fraction that is to be ingested is not colostrum, but a specific fraction of colostrum. As previously argued, the composition has been prepared by a specific process and as a consequence, certain factors are maintained which allow the colostrum product to change physical work capacity. The specific composition contains casein and is treated by spray drying which preserves the essential ingredients which can assist in achieving the results indicated. It is the specific combination that remains after this process that derives the advantages of the colostrum product. It is proposed that the casein may assist in preserving the essential components particularly in the gut after ingestion. The prior art such as Clark *et al.* teaches removal of casein and as such is a different composition. Similarly, the newly cited prior art namely WO 97/43905 also removes casein. In fact, casein is considered to be problematic when processing colostrum. Furthermore, spray drying is not a process that is generally used in processing colostrum. Therefore the combination of casein and spray drying colostrum after ultrafiltration results in a unique colostrum product. The colostrum

product is still expected to contain various growth factors and proteins that are generally found in colostrum and these may contribute to the changing of physical work capacity.

It is not expected that the colostrum product would work if it was ingested. Any proteins or growth factors that are present in the colostrum would be degraded in the gut and thereby have no effect on changing physical work capacity. Moreover, any growth factors would be considered too large to cross into the blood stream. However, the colostrum composition of the present invention does have an effect as evidenced by the Examples and from the Declaration by Jon Buckley which was submitted previously. This is indeed an unexpected result for an orally administered colostrum product.

The Examiner's obviousness objection results from collating the five citations. The reasoning behind the objection is that colostrum can be processed in the manner outlined in the claim (especially AU-A-63136/94) to remove bacteria and because colostrum can be useful for muscle protection or for reducing muscular recovery (WO 97/43905) the Examiner considered it is obvious that any processed colostrum would do the same. The Examiner is also of the opinion that IGF-1 present in the colostrum may contribute to this improved performance. Introducing more process steps known to the skilled addressee does not make the use of a colostrum fraction any less obvious because it is still processed colostrum. The Examiner appears to be of the opinion that any processed colostrum can be used to improve physical work capacity and that all types of processed colostrum will be the same.

The Examiner then concludes that there is no unexpected successful result using any processed colostrum, particularly since IGF-1 is expected to be present. Previously, the Examiner relied on Clark *et al.* and since it was

argued that it is not credible and would not be accepted on clear review, the Examiner has therefore relied on WO 97/43905 to support an improved ability to do more exercise and improve recovery from exercise.

Applicants submit that the Examiner has not taken appropriate consideration of the application, prosecution history file and references.

I. The colostrum fraction is unique.

The colostrum fraction is unique; as it has been processed with specific steps (see above) and thereby results in a specific combination of components. The result is a different colostrum fraction to that which has been used in WO 97/43905. When used together, the components provide the advantages for oral administration to improve exercise performance. The presence of IGF-1 has previously been proven by Jon Buckley in his Declaration (submitted previously) to have no effect. For that reason, applicants have stated that there is no detectable change in plasma IGF-1.

II. IGF-1 has no effect nor is there a detectable change in concentration.

The Examiner has not taken into consideration that IGF-1 (a protein) will generally be degraded by enzymes in the stomach. IGF-1 used by athletes will generally be systemically injected. The application is therefore quite different, as high concentrations of IGF-1 can be applied systemically compared to orally and affect exercise performance.

III. The colostrum fraction in the invention contains casein.

The Examiner's reliance on WO 97/43905 instead of Clark *et al.* is flawed since the colostrum milk product has casein removed. The citation is therefore not relevant as it relates to a different fraction of colostrum to that of the present invention which

proposes specifically to retain casein. As discussed above, certain advantages are obtained by maintaining casein but casein is considered to be generally problematic when processing colostrum. Therefore it is generally removed in the processing of colostrum.

IV. The newly cited reference WO 97/43905 uses a colostrum fraction without casein and therefore, the reference is not relevant.

This reference provides a colostral fraction devoid of casein.

Despite a description of it being used as a food supplement for muscle protection or for reducing the muscular recovery phase and for the prevention and treatment of bacterial, viral and mycotic infections, and in a oral way, the colostral milk product is different to that used in the present invention which retains casein.

In fact, the uses of this product included in claims 16-20 of WO009743905A1 (see below) where the closest claim to the present invention is for the use for the protection of muscle cells, for shortening the muscular recovery period, etc. in claim 20. This is different from the use in the present invention.

16. Use of a colostral milk product according to at least one of claims 10 to 14 as a medicament, food supplement or cosmetic preparation.

17. Use of a colostral milk product according to at least one of claims 10 to 14 as an additive for medicaments, food supplements, beverages or cosmetic preparations.

18. Use according to claim 17, **characterized in that** the colostral milk product is used as an ingredient of baby food, dietetic food, clinical food, in particular

food for tube feeding.

19. Use according to claim 17, **characterized in that** the colostral milk product is used as a medicament for at least supporting treatment of neurodermatitis, wound healing, rheumatoid conditions, allergies, in particular hay fever, pollen allergies; cardiac infarctions and muscle ailments during rehabilitation, and for supporting treatment of liver and bone ailments.

20. Use according to claim 17, **characterized in that** the colostral milk product is used for the protection of muscle cells, for shortening the muscular recovery period, for prophylaxis and support in viral bacterial and mycotic infections, and for fortifying the immune system.

In fact the only described use of the colostrum that is actually tested in the patent specification relates to neurodermitis. No effects are shown in the specification for uses as in claim 20 for protecting muscle cells or shortening the muscular recovery period. Furthermore as stated above casein has been removed.

The citation is not relevant to combine with the other citations since the fraction does not contain casein and does not apply the colostrum fraction to improving physical work capacity, nor does it show that it could have any effect on muscle development.

The difference between casein being present or absent.

To determine whether the citations raised by the Examiner render the claims obvious requires that the citations must contribute to a suggestion that the invention was obvious and that there would be no surprising or unexpected effects in the light of these citations.

The citations cited by the Examiner give no reason to believe that the composition would have an effect on physical work capacity and The result is surprising in the light of what has been tried before and in the light of inconsistent test results from which conclusions are drawn. It is submitted that the citations are not relevant and the Examiner has evaluated the claims in hindsight.

Prior Art Colostrum Fractions compared with the Present Invention

In the prior art, it is taught to remove casein. Its absence is not considered to have any impact on the ability of the colostrum fraction to perform and specifically to effect athletic performance.

The colostrum fraction in the prior art is a whey product formed from the filtrate of the casein removed ultra filtered colostrum whey. In contrast, the present invention utilizes a retentate of ultra filtered colostrum including casein and whey protein. The prior art teaches that the effective components of colostrum are found in the whey.

The thinking at the time (priority date 1998) was that the “biological value” of whey protein was higher than casein protein. Growth factors are mostly found in the whey fraction. Hence the focus was on the whey fractions rather than casein fractions.

Milk whey was also seen to be superior to milk casein (and other protein sources) for performance due to rapid changes in protein synthesis (Boirie *et al* 1997 - attached). The present applicants have therefore taken a contrary approach, which was not obvious at the time and retained the casein fraction with the whey.

No prior citation provides any incentive to pursue the casein route and in fact, discards this as a contaminant and of no beneficial outcome.

The art at the time also encouraged discarding fat, casein and sugar to maximise the concentration of the bioactive growth factors in the whey which were expected to provide the performance benefit.

IGF – 1 and Muscle Power

Prior to 1998 the hypothesis for performance improvement with colostrum, (Mero *et*

al 1997) was to focus on the putative effects of IGF-1, which is found in the whey portion of protein, and to use colostrum whey rather than milk whey due to higher concentrations of growth factors in colostrum.

Results in Mero *et al* show that there is an increase in IGF-1 and insulin by using Bioenervi®, a colostrum whey product, compared with normal milk whey in the individuals tested. The conclusion was that bovine colostrum supplement (Bioenervi®) increases serum IGF-1 concentration in athletes during strength and speed training. However, despite the increased IGF-1 there was no measurable training effect in jumping performance (last sentence of Results).

The general expectation of the bovine colostrum whey fraction in these citations is that it would have a positive effect on human tissue during strenuous training thereby having a beneficial effect on physical work capacity. Hence there is an expectation in the prior art that a colostrum composition prepared in the same way (which is absent casein) will have an impact on physical performance. Conversely, a colostrum fraction which is not prepared the same way may not have the same impact.

The bovine colostrum fraction of the present invention shows that an increase in the plasma IGF-1 concentration was not detectable. Hence it would be expected that without a detectable increase in IGF-1 concentration muscle power would not increase and hence physical work capacity would not change.

Surprisingly the bovine colostrum fraction which contains casein and which is produced by the methods outlined shows significant improvement in vertical jumping performance (example 4), distance covered and the amount of work done during a second treadmill run (example 2); despite there being no significant IGF-1 increase. Hence, this amounts to increased total work done as a result of the colostrum fraction of the present invention. Accordingly, it submitted that since the bovine colostrum fraction causes no increased concentration of IGF-I, it is surprising that a significant increase in the physical activity was experienced.

The results of the studies of the present invention were published in 1999 and despite no increase in IGF-1 but improved performance, researchers in this area such as Mero *et al* continued to pursue colostrum whey filtrate which had showed an increase in circulating IGF-1. The presence of casein was not seen to be beneficial to the improvement of performance because the colostrum whey product itself had shown increase in circulating IGF-1 which was seen to be crucial in improving performance. A product which does not elicit the same increase in IGF-1 was not expected to work and yet surprisingly it did!

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1. At the priority date (1998) the person skilled in the art was of the understanding that the “biological value” of whey protein was higher than casein protein and that growth factors were found in the whey. Hence there was an increasing focus on the benefits of whey protein over and above other protein sources for possible strength and performance benefits.

2. Prior art teaches removal of casein suggesting that casein has no expected effect on physical work capacity. When compared against whey, the colostrum product of the present invention provides surprising results for vertical jumping performance, distance covered and the amount of work done during a second treadmill run (see example 2 and 4).

3. Prior to 1998, IGF-1 was the focus for improved performance from colostrum whey. However, IGF-1 levels were not found to increase in the tests conducted for the present invention. Nevertheless, there were improvements in performance. Mero *et al* teaches increased IGF-1 and expected an increase in physical work capacity. Increases in IGF-1 do not contribute to improved performance and colostrum whey does not improve performance despite and increase in IGF-1.

4. Athletes who train for a long time show reduction in immune capacity. This impacts on their work capacity. Casein is associated with allergies and impacts on work capacity. Because of this, maintaining casein in the bovine colostrum product and administering to athletes with a compromised immune system would not be expected to be beneficial for the reason that it is associated with allergies. However, surprisingly the bovine colostrum product of the present invention (containing casein) had no effect on the athletes but improved their vertical jumping performance, distance covered and the amount of work done during a second treadmill run.

Therefore, as no combination of the reference make the claims obvious, it is respectfully requested that the rejection be withdrawn.

It is submitted that the application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Janet I. Cord', with a long horizontal line extending to the right.

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